NIH NATIONAL CANCER INSTITUTE

INCREASED THERAPEUTIC EFFECTIVENESS OF PE-BASED IMMUNOTOXINS

SUMMARY

To improve the therapeutic effectiveness of PE-based immunotoxins through multiple rounds of drug administration, NIH inventors have sought to identify and remove the human B cell epitopes within PE. Previous work demonstrated that the removal of the murine B cell and T cell epitopes from PE reduced the immunogenicity of PE and resulted in immunotoxins with improved therapeutic activity. The National Cancer Institute's Laboratory of Molecular Biology seeks interested parties to co-develop and commercialize immunotoxins using toxin domains lacking human B cell epitopes.

REFERENCE NUMBER

E-263-2011

PRODUCT TYPE

- Therapeutics

KEYWORDS

- Chemotherapy
- Immunotoxin
- Immunogenic epitopes
- Human B cell epitopes
- Pseudomonas Exotoxin A
- B-Cell, T-cell

COLLABORATION OPPORTUNITY

This invention is available for licensing and co-development.

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DESCRIPTION OF TECHNOLOGY

Patients receiving immunotoxin cancer therapy are less likely to experience the deleterious side-effects associated with non-discriminate therapies such as chemotherapy or radiation therapy. Unfortunately, the continued administration of immunotoxins often leads to a reduced patient response due to the formation of neutralizing antibodies against immunogenic epitopes contained within Pseudomonas exotoxin A (PE).

To improve the therapeutic effectiveness of PE-based immunotoxins through multiple rounds of drug administration, NIH inventors have sought to identify and remove the human B cell epitopes within PE. Previous work demonstrated that the removal of the murine B cell and T cell epitopes from PE reduced the immunogenicity of PE and resulted in immunotoxins with improved therapeutic activity.

This technology involves the identification and removal of major human B cell epitopes on PE by mutation or deletion. Considering these immunotoxins will be administered to humans, the removal of human immunogenic epitopes is important. The resulting PE-based immunotoxins have increased resistance to the formation of neutralizing antibodies, and are expected to have improved therapeutic efficacy.

POTENTIAL COMMERCIAL APPLICATIONS

- Treatment of diseases associated with increased or preferential expression of a specific cell surface receptor such as hematological cancers, lung cancer, ovarian cancer, breast cancer, and head and neck cancers

COMPETITIVE ADVANTAGES

- PE variants now include the removal of human B-cell epitopes, further reducing the formation of neutralizing antibodies against immunotoxins which contain the PE variants
- Less immunogenic immunotoxins result in improved therapeutic efficacy by permitting multiple rounds of administration in humans
- Targeted therapy decreases non-specific killing of healthy, essential cells, resulting in fewer non-specific side-effects and healthier patients

INVENTOR(S)

- Ira Pastan, MD (NCI)

DEVELOPMENT STAGE

- Discovery (Lead Identification)

PATENT STATUS

- **U.S. Filed:** U.S. Patent Application No. 14/927,645 filed October 30, 2015
- **Foreign Filed:** European Patent Application No. 12766780.6 filed February 28, 2014

RELATED TECHNOLOGIES

- E-269-2009 - Improved PE-based Targeted Toxins: A Therapeutic with Increased Effectiveness
- E-292-2007
- E-262-2005

THERAPEUTIC AREA

- Cancer/Neoplasm